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EXAMINER

LAMBERTSON, DAVID A

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 01/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/758,036

Applicant(s)

LEBERER ET AL.

Examiner

David A. Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-10, 20, 21 and 25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10, 20, 21 and 25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_

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### DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed November 5, 2004. Amendments were made to the claims.

Claims 1-10, 20, 21 and 25 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, mailed May 6, 2004, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Graber in view of Ketchum and Fairman as recited in the previous Office Actions. **This rejection is maintained for the reasons set forth in the previous Office Action.**

Claims 1-3, 20, 21, 4-10\* and 25\* are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaber in view of Ketchum and Fairman as applied to claims 1-3, 20 and 21 above, and further in view of Tang and Rampe, as set forth in the previous Office Actions.

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(Note-\* indicate claims rejected in view of the additional references). **This rejection is maintained for the reasons set forth in the previous Office Action.**

***Response to Arguments Concerning Claim Rejections - 35 USC § 103***

Applicant's arguments filed November 5, 2004 have been fully considered but they are not persuasive. Applicant provides the following grounds of traversal:

1. It is argued that “one of [ordinary] skill in the art, with full knowledge of Graber, Ketchum et al and Fairman et al, would not have had a reasonable expectation of success in using the triple deletion mutants of Fairman et al as a substitute for the double deletion mutants in the Graber complementation assay.” This is allegedly because “as the pathology associated with the inactivation of endogenous genes becomes more severe, complementation assays become more difficult,” and “it becomes less and less likely that the heterologous gene added...can sufficiently reverse that pathology to provide any meaningful assay results” (see for example page 6, second paragraph of Applicant’s response).
2. It is argued that, although Graber teaches that a heterologous eukaryotic potassium ion channel is capable of complementing a yeast strain deleted for *TRK1* and *TRK2*, there is no way of predicting that said heterologous eukaryotic potassium ion channel would be capable of complementing a yeast strain deleted for *TRK1*, *TRK2* and *TOK1*. Allegedly, this is because the triple deletion phenotype is more severe than the double deletion phenotype (see for example page 6, third paragraph of Applicant’s response).

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3. It is argued that the addition of Tang and Rampe does not abrogate the lack of a reasonable expectation of success provide in the rejection under Graber in view of Ketchum and Fairman alone (see for example page 7, first paragraph of Applicant's response).

Applicant's arguments have been considered, but are not found convincing for the following reasons:

1. First, the allegation of a lack of a reasonable expectation of success is based solely on the opinion of Applicant, and is not supported by any evidence to the contrary. There is no scientific support the statement: "as the pathology associated with the inactivation of endogenous genes becomes more severe, complementation assays become more difficult... it becomes less and less likely that the heterologous gene added... can sufficiently reverse that pathology to provide any meaningful assay results." Indeed, when consulting the art, the ordinary skilled artisan would recognize the benefit of as increased pathology of a given strain, and that it forms the basis for complementing the strain. This is in direct contrast to Applicant's statement of opinion.

Takekawa teaches a yeast-based complementation assay to identify a human homolog of MAP kinase kinase kinases (MAPKKK). In this assay, the yeast strain that is used is a triple deletion strain (*ssk2Δ ssk22Δ sho1Δ*) that has an increased pathology over any given double deletion combination (*ssk2Δ ssk22Δ*, *ssk22Δ sho1Δ* or *ssk2Δ sho1Δ*); this is acknowledged by Takekawa who recognizes that "any one of the functional *SSK2*, *SSK22* and *SHO1* genes is sufficient to suppress the osmosensitivity of the triple mutants" (see for example page 4974, left column last paragraph). In other words, the triple mutant and its increased pathology is necessary to obtain proper complementation.

Thus, it is clear from the evidence in the art that complementation does not necessarily become “less likely” or “more difficult” to achieve when the pathology increases (as Applicant alleges). Rather, the skilled artisan would recognize that when an third endogenous gene (e.g., *SHO1* as presented in the evidence, or *TOK1* in the instant case) is present that can achieve the same function as two other genes that are already deleted (such as *SSK2* and *SSK22* in the evidence, or *TRK1* and *TRK2* in the instant case), it is preferable to delete that third gene in order to avoid interference from the third gene in the complementation. Given this evidence, the allegation that there would be no expectation of success based on the severity of a phenotype does not appear to agree with logical scientific rationale, and is insufficient to overcome the rejection.

2. The combination of references for the instant rejection is the same as the situation in Takekawa (which was successfully implemented), where a triple deletion is provided to accurately allow for the complementation of a phenotype by a heterologous gene. In the instant case, Graber teaches an assay involving the deletion of *TRK1* and *TRK2* from a cell, where a heterologous potassium ion channel is expressed to overcome the phenotype of *TRK1* and *TRK2*. However, Ketchum and Fairman teach that there is a third gene that can endogenously complement the deletion of *TRK1* and *TRK2*. Given the pattern seen in the prior art as exemplified by Takekawa, wherein a triple deletion of three genes with a common function was used to accurately represent the complementation of a phenotype, the ordinary skilled artisan would have had a reasonable expectation of success when combining the references of Graber, Ketchum and Fairman to construct a *trk1Δ trk2Δ tok1Δ* strain to allow accurate complementation of the strain by a heterologous potassium ion channel.

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3. The argument that Tang and Rampe do not abrogate the lack of a reasonable expectation of success alleged for the combination of Graber in view of Ketchum and Fairman is moot because no such abrogation is necessary, given that a reasonable expectation of success is indeed found within that combination of references.

In conclusion, Applicant has provided an argument that there was no expectation of success when combining Graber, Ketchum and Fairman. Applicant offers the opinion that “as the pathology associated with the inactivation of endogenous genes becomes more severe, complementation assays become more difficult... it becomes less and less likely that the heterologous gene added...can sufficiently reverse that pathology to provide any meaningful assay results.” However, in response to this opinion, the Office has provided evidence that, in similar situations (e.g., Takekawa) where there is a third gene that can accomplish the function of two genes that have been deleted, it is preferable to delete the third gene in order to allow for proper complementation. Because the Office has provided evidence that there is an expectation of success for combining references such as Graber, Ketchum and Fairman, Applicant’s traversal is not found convincing and the rejection is maintained.

***Allowable Subject Matter***

No claims are allowable.

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**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.  
AU 1636



**JAMES KETTER**  
**PRIMARY EXAMINER**